Department of Defense

DIRECTIVE

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Administrative Reissuance Incorporating Through Change 2, July 20, 1983

USDR&E

SUBJECT: Protection of Human Subjects in DoD-Supported Research

References: (a) Department of Health and Human Services Regulation, "Protection of Human Subjects," (45 CFR 46)
(b) Food and Drug Administration Regulation (21 CFR subchapters A, D, and H)
(c) DoD Instruction 5030.29, "Investigational Use of Drugs by the Department of Defense," May 12, 1964 (hereby canceled)
(d) DoD Directive 6000.4, "Clinical Investigation Program," April 16, 1976
(e) Memorandum of Understanding Between the Food and Drug Administration and the Department of Defense, "Investigational Use of Drugs by the Department of Defense," November 21, 1974

1. PURPOSE

This Directive, under references (a) and (b), establishes policy; assigns responsibilities; specifies authority for protecting the rights and welfare of humans used as subjects of study in DoD-supported research, development, test, and evaluation (RDT&E) and clinical investigation activities (hereafter referred to as "research"); and cancels reference (c).

2. APPLICABILITY AND SCOPE

2.1. This Directive applies to the Office of the Secretary of Defense (OSD), the Military Departments, the Organization of the Joint Chiefs of Staff, the Unified and Specified Commands, the Defense Agencies, and the Uniformed Services University

of the Health Sciences (USUHS) (hereafter referred to as the "DoD Components") and to contractor or grantee activities supported by the Department of Defense.

2.2. Its provisions encompass the following:

2.2.1. Clinical investigations as established by reference (d), biomedical research, and behavioral studies.

2.2.2. RDT&E involving new drugs, vaccines, biologicals, or investigational medical devices.

2.2.3. Inclusion of human subjects, whether as the direct object of research or as the indirect object of research involving more than minimal risk in the development and testing of military weapon systems, vehicles, aircraft, and other materiel. The determination of whether a research protocol involves more than minimal risk shall be made by review committees established in accordance with section 6., below. Nothing in this Directive is intended to supersede requirements for health hazard or other safety reviews required by other DoD issuances or other DoD Component regulations.

2.3. Its provisions do not apply to epidemiological surveys that are of no more than minimal risk as set forth in the human protection regulations issued by the Department of Health and Human Services (45 CFR 46, reference (a)).

2.4. Nothing in this Directive is intended to limit the authority of a healthcare practitioner to provide emergency medical care under applicable law of the jurisdiction in which the care is provided or of commanders in the discharge of assigned duties or responsibilities.

3. DEFINITIONS

Terms used in this Directive are as defined in reference (a), except for the following:

3.1. Human Subject. A living individual about whom an investigator conducting research obtains data through interaction with the individual, including both physical procedures and manipulations of the subject or the subject's environment. The term does not include military or civilian personnel who are qualified to test by assignment to duties that call specifically for such qualifications such as test pilots and test engineers.

3.2. Non-U.S. Citizens. Foreign nationals, excluding, for the purposes of this Directive, personnel on active duty.

3.3. Research. A systematic investigation as described in paragraphs 2.2.1., 2.2.2., and 2.2.3., above, that is designed to develop or contribute to generalizable knowledge. The term does not include individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercises.

4. POLICY

4.1. It is the policy of the Department of Defense that:

4.1.1. The fundamental rights and welfare of human subjects in research funded by DoD Components shall be protected to the maximum extent possible. This protection is meant to encompass basic respect for human dignity and to protect subjects from actual harm. Responsibility for the protection of human subjects is a command responsibility.

4.1.2. Except as provided elsewhere in this Directive, the human protection regulations issued by the Department of Health and Human Services (reference (a)) shall apply to research supported by the Department of Defense.

4.1.3. Contractors or grantees (and elements of DoD Components) holding an assurance of compliance with the human use regulations of the Department of Health and Human Services (45 CFR 46, reference (a)) shall be considered in compliance with the terms of this Directive. In the absence of such an assurance, a special assurance that meets the minimum requirements of reference (a) shall be negotiated between the contractor or grantee and the DoD Component concerned.

4.1.4. Only persons who are informed fully and voluntarily agree to participate *may be used as human subjects in research. The only exception to the policy is that consent to participate may be obtained from a legal representative of the subject when the measures used are intended to be beneficial to the subject.*

4.1.4.1. In research conducted outside the United States involving non-U.S. citizens as human subjects, the laws, customs, and practices of the country in which the research is conducted, or those required by this Directive, whichever are more stringent, shall take precedence. The research shall meet the same standards of

ethics and safety that apply to research conducted within the United States involving U.S. citizens.

4.1.4.2. The use of prisoners of war as human subjects of research is prohibited.

4.1.5. For any research involving human subjects, a medical monitor shall be appointed by name if the approving official determines that the risk is more than minimal.

4.2. Requests for exceptions to policy as stated above shall be submitted with full justification to the Under Secretary of Defense for Research and Engineering (USDR&E) by Heads of DoD Components.

5. RESPONSIBILITIES

5.1. The Under Secretary of Defense for Research and Engineering, or designee, shall:

5.1.1. Develop policies in coordination with the Assistant Secretary of Defense (Health Affairs) (ASD(HA)) to protect human subjects in DoD-funded research.

5.1.2. Coordinate DoD Component activities in the protection of human subjects.

5.1.3. Serve as the point of contact within the Department of Defense and act as the principal DoD liaison with civil or Federal Agencies outside the Department of Defense on matters pertaining to protection of humans in research.

5.1.4. Serve as the final DoD approval authority for all research involving actual exposure of human subjects to nuclear weapons effect or chemical warfare agents.

5.2. The Assistant Secretary of Defense (Health Affairs) shall:

5.2.1. Provide policy guidance regarding medical safety and standards of professional medical care and conduct as they relate to the use of humans in research.

5.2.2. Serve as the DoD representative on matters relating to implementation of Food and Drug Administration (FDA) regulatory requirements.

5.3. The Heads of DoD Components, or designees, shall:

5.3.1. Protect the rights and welfare of human subjects in research sponsored or conducted by or among the members of the respective DoD Components.

5.3.2. When more than one DoD Component is involved, determine primary responsibility based upon consideration of whether the subjects are inpatients or outpatients of a DoD medical treatment facility (MTF); whether the research is conducted in-house or by contract; or whether the prospective human subjects are members of a DoD Component.

5.3.2.1. When the research, regardless of in-house or contract status, involves use of patients of a DoD MTF, the Component to which the MTF belongs organizationally shall have primary responsibility, except as provided in subsection 5.5., below.

5.3.2.2. For research not involving the use of patients at a DoD MTF, primary responsibility rests as follows:

5.3.2.2.1. If the research is done on grant or contract, primary responsibility rests with the DoD Component providing funds.

5.3.2.2.2. If the research is conducted in-house, primary responsibility rests with the DoD Component to which the principal investigator is assigned.

5.3.2.2.3. If the research is not funded by a DoD Component and there is no DoD principal investigator, primary responsibility rests with the DoD Component to which the prospective human subject is assigned.

5.3.3. Establish procedures to maintain adequate documentation of human subjects used in research, including resulting adverse reactions.

5.3.4. Establish procedures for responding to reports of improper use of human subjects.

5.3.5. Establish review committees as provided for in subsection 6.2., below.

5.4. The Secretaries of the Military Departments shall approve in-house and contract research involving human subjects, conducted at or funded by a DoD Component for which the Military Department has been designated executive agent.

This responsibility includes research that is classified for reasons of national security. When more than one Military Department is involved in the same research, the first review committee to which the research is submitted shall perform the human use review and make recommendations to the Military Department Secretaries concerned. Each Secretary may accept these recommendations or may require additional reviews.

5.5. The President, Uniformed Services University of the Health Sciences, and the Director, Defense Nuclear Agency (DNA), shall have primary responsibility for research by their respective DoD Components when the research does not also involve patients of a DoD MTF. The President, USUHS, shall have additional responsibility for research conducted in-house or by contract when the research involves patients of a DoD MTF or other U.S. Government healthcare facility, and USUHS directly funds the research, has received a grant or gift, or has received some other non-DoD form of support for the research. However, in these instances, the MTF review committee shall perform the human use review and make recommendations to the President, USUHS, and to the DoD Component or other U.S. Government institution concerned. The President, USUHS, may accept these recommendations or may require additional reviews.

6. PROCEDURES

6.1. Delegation of Authority

6.1.1. The Secretaries of the Military Departments are authorized to delegate all or part of their authority under section 5., above, within the military chain of command to the lowest level operating a human-subjects review process.

6.1.2. In addition, the Secretaries of the Military Departments are authorized to make the determination that unique military requirements dictate the use of drugs or devices not officially approved by the FDA. The Secretaries of the Military Departments may delegate this authority to the respective Surgeons General or designees.

6.1.3. The President, USUHS, may delegate the authority specified in subsection 5.5., above, to the Dean or Associate Deans.

6.1.4. Requests for approval of the use of human subjects in research funded by DoD Components other than the Military Departments, DNA, and USUHS shall be submitted to the USDR&E for final determination.

6.1.5. Authority not delegated above to specific officials is retained by the Secretary of Defense.

6.2. Review Committees. Each official having approval authority for research involving human subjects shall establish one or more committees to provide initial and continuing review of the use of human subjects in such research.

6.2.1. The review committee is similar functionally to the Institutional Review Board (IRB) established under 45 CFR 46, (reference (a)). The IRB performs protocol review and protocol approval. Within the Department of Defense these functions are separated. Review committees exercise only protocol review and recommend approval, modification, or disapproval to an approving authority. Approval authority is vested in the approving official to whom the review committee reports.

6.2.2. The review committee shall be constituted in accordance with reference (a) standards for IRBs and paragraph 5.3.5., above, with the following exceptions:

6.2.2.1. The prohibition in reference (a) of all-male or all-female membership may be waived by the approving official when compliance is impractical.

6.2.2.2. The requirement in 45 CFR 46 (reference (a)) for a nonaffiliated member may be met by appointment of a member of an institution or organizational unit not subject to the immediate authority of the approving official.

6.2.2.3. When the approving authority, or the review committee itself, has reason to believe a given proposal includes more than minimal risk, a physician shall be included as an ad hoc member of the committee (see also paragraph 4.1.5., above).

6.2.2.4. The approving official may not be a member.

6.2.3. The review committee shall retain records of research reviewed for at least 3 years after the completion of the research, or at the option of the approving official, shall forward records to that official for longer retention.

6.2.4. An approving official may not approve research for which the official is also a principal or coinvestigator. Such research shall be reviewed and approved at a higher echelon of command.

6.2.5. Research that involves the use of human subjects may not be initiated until all necessary approvals and the informed consent of the subjects have been obtained.

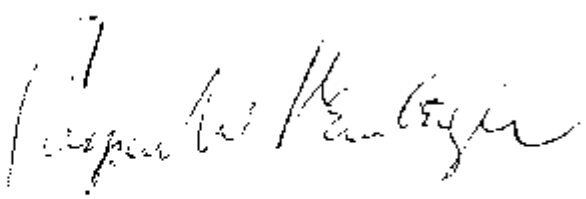
6.2.6. If a review committee recommends safeguards or special conditions to a protocol it is recommending for approval, the approving official may not reduce the safeguards or conditions upon approving the protocol. The approving official may require additional safeguards, may disapprove the protocol, or may refer it to a higher approving authority and review committee.

7. INFORMATION REQUIREMENTS

The memorandum of understanding between the FDA and the Department of Defense (reference (e)) requires that the FDA be informed whenever the use of human subjects in new drug or device research that is classified for reasons of national security has been approved. The FDA also shall be informed when a determination has been made that unique military requirements dictate the use of drugs or devices that have not been approved by the FDA. Such notification also shall be provided to the USDR&E and ASD(HA).

8. EFFECTIVE DATE AND IMPLEMENTATION

This Directive is effective immediately. Forward two copies of implementing documents to the Under Secretary of Defense for Research and Engineering within 180 days.



Caspar W. Weinberger
Secretary of Defense